

AMENDED CLAIMS

[received by the International Bureau on 17 April 2003 (17.04.03);
Claims 1 replaced by new claim 1; remaining claims unchanged]

1. A compound having the following formula:



wherein:

5 Ar is a 1-(sulfonyl)-1H-indol-2-yl group;

the group -OR⁰ is independently:

- (a) -OH;
- (b) an ether group; or:
- (c) an acyloxy group;

10 the bond marked α is independently:

- (a) a single bond; or:
- (b) a double bond;

the bond marked β is independently:

- (a) a single bond; or:
- (b) a double bond;

15 each of R², R³, R⁵, and R⁶, is independently a ring substituent and is:

- (a) H;
- (b) a monovalent monodentate substituent; or:
- (c) a ring substituent which, together with an adjacent ring

20 substituent, and together with the ring atoms to which these ring substituents are attached, form a fused ring;

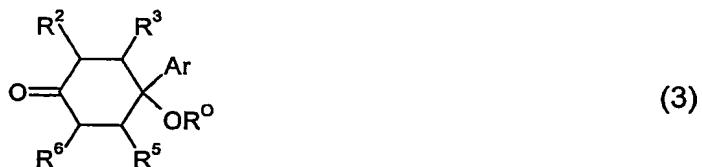
and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.

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2. A compound according to claim 1, wherein α is independently a double bond and β is independently a double bond, and the compound has the following formula:



5 3. A compound according to claim 1, wherein α is independently a single bond and β is independently a single bond and the compound has the following formula:



10 4. A compound according to claim 1, wherein α is independently a single bond and β is independently a double bond, and the compound has the following formula:



15 5. A compound according to any one of claims 1 to 4, wherein said monovalent monodentate substituent is selected from:

hydroxy (-OH);

halo;

cyano (-CN);

carboxy (-COOH);

azido;

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ester;

amino, including:

C₁₋₇alkyl-amino;

amino-C₁₋₇alkyl-amino;

5 C₁₋₇alkyl, including:

halo-C₁₋₇alkyl;

amino-C₁₋₇alkyl;

carboxy-C₁₋₇alkyl;

hydroxy-C₁₋₇alkyl;

10 C₅₋₂₀aryl-C₁₋₇alkyl;

ether, including:

C₁₋₇alkoxy;

halo-C₁₋₇alkoxy;

amino-C₁₋₇alkoxy;

15 carboxy-C₁₋₇alkoxy;

hydroxy-C₁₋₇alkoxy;

C₅₋₂₀aryl-C₁₋₇alkoxy;

acyl, including:

C₁₋₇alkyl-acyl;

20 halo-C₁₋₇alkyl-acyl;

amino-C₁₋₇alkyl-acyl;

carboxy-C₁₋₇alkyl-acyl;

hydroxy-C₁₋₇alkyl-acyl;

C₅₋₂₀aryl-C₁₋₇alkyl-acyl;

25 C₅₋₂₀aryl-acyl;

C₅₋₂₀aryl;

thiol (-SH); and,

thioether.

30 6. A compound according to any one of claims 1 to 4, wherein said monovalent monodentate substituent is selected from:

-OH;

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- F, -Cl, -Br, -I;
- CN;
- COOH;
- N₃;
- 5 -COOMe, -COOEt, -COOtBu, -COOPh, -COOCH₂Ph;
- NH₂, -NHMe, -NHEt, -NMe₂, -NEt₂;
- piperidino, morpholino, piperazino, N-methyl-piperazino;
- NH(CH₂)_w-NH₂, -NH(CH₂)_w-NHMe, -NH(CH₂)_w-NMe₂, -NH(CH₂)_w-NEt₂;
- 10 -Me, -Et, -nPr, -iPr, -nBu, -iBu, -sBu, -tBu;
- CH₂F, -CH₂Cl, -CF₃, -CCl₃, -CF₂CF₃, -CH₂CF₃, -C(CF₃)₃;
- CH₂NH₂, -(CH₂)_w-NHMe, -(CH₂)_w-NMe₂, -(CH₂)_w-NEt₂;
- CH₂COOH;
- 15 -(CH₂)_w-OH;
- CH₂Ph;
- OMe, -OEt, -OnPr, -OiPr, -OnBu, -OiBu, -OsBu, -OtBu;
- OCH₂F, -OCH₂Cl, -OCF₃, -OCCl₃, -OCF₂CF₃, -OCH₂CF₃, -OC(CF₃)₃;
- 20 -O(CH₂)_w-NH₂, -O(CH₂)_w-NHMe, -O(CH₂)_w-NMe₂, -O(CH₂)_w-NEt₂;
- O(CH₂)_w-COOH;
- O(CH₂)_w-OH;
- OCH₂Ph;
- 25 -C(=O)Me, -C(=O)Et, -C(=O)-nPr, -C(=O)-iPr, -C(=O)-nBu, -C(=O)-iBu, -C(=O)-sBu, -C(=O)-tBu;
- C(=O)CH₂F, -C(=O)CH₂Cl, -C(=O)CF₃, -C(=O)CCl₃, -C(=O)CF₂CF₃, -C(=O)CH₂CF₃, -C(=O)C(CF₃)₃;
- C(=O)(CH₂)_w-NH₂, -C(=O)(CH₂)_w-NHMe, -C(=O)(CH₂)_w-NMe₂,
- 30 -C(=O)(CH₂)_w-NEt₂;
- C(=O)(CH₂)_w-COOH;
- C(=O)(CH₂)_w-OH;
- C(=O)CH₂Ph;

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-Ph;

-SH;

5 -SMe, -SEt, -SnPr, -S-iPr, -S-nBu, -S-iBu, -S-sBu, -S-tBu,
 -S-CH₂-Ph, -S-Ph;
 a thioether group derived from cysteine, homocysteine, glutathione, or a peptide comprising the sequence -Cys-(X)_y-Cys-, where X is an amino acid, and y is an integer from 1 to 6;

10

wherein w is an integer from 1 to 7.

* * *

15 7. A compound according to any one of claims 1 to 6, wherein each of R², R³, R⁵, and R⁶, is independently a ring substituent and is:
 (a) H; or:
 (b) a monovalent monodentate substituent.

20 8. A compound according to any one of claims 1 to 6, wherein R⁵ and R⁶ are -H; but R² and R³ do not also form a fused ring:



9. A compound according to any one of claims 1 to 6, wherein R² and R³ are -H; but R⁵ and R⁶ do not also form a fused ring:



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10. A compound according to any one of claims 1 to 6, wherein R² and R⁶ are -H:



11. A compound according to any one of claims 1 to 6, wherein R³ and R⁵ are -H:



12. A compound according to any one of claims 1 to 6, wherein R², R³, R⁵ and R⁶ are -H:



10 13. A compound according to any one of claims 1 to 6, wherein R², R³, R⁵ and R⁶ are -H; α is a double bond; and β is a double bond:



14. A compound according to any one of claims 1 to 6, wherein R², R³, R⁵ and R⁶ are -H; α is a single bond; and β is a single bond:



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15. A compound according to any one of claims 1 to 6, wherein R², R³, R⁵ and R⁶ are -H; α is a single bond; and β is a double bond:



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16. A compound according to any one of claims 1 to 6, wherein

- (a) R² and R³, together with the ring atoms to which they are attached, form a fused ring;
- (b) R⁵ and R⁶, together with the ring atoms to which they are attached, form a fused ring; or
- (c) or both (a) and (b).

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17. A compound according to claim 16, wherein the fused ring, or, if there are two fused rings, one of them, or each of them, is a fused aromatic ring.

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18. A compound according to claim 16, wherein the fused ring, or, if there are two fused rings, one of them, or each of them, is a fused aromatic ring with 5 or 6 ring atoms.

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19. A compound according to claim 16, wherein R² and R³ form a fused benzene ring; and β is a double bond:



20. A compound according to claim 19, wherein R⁵ and R⁶ do not also form a fused ring.

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21. A compound according to claim 16, wherein R² and R³ form a fused benzene ring; β is a double bond; and R⁵ is -H:



5 22. A compound according to claim 16, wherein R² and R³ form a fused benzene ring; β is a double bond; and R⁶ is -H:



23. A compound according to claim 16, wherein R² and R³ form a fused benzene ring; β is a double bond; and R⁵ and R⁶ are -H:



10 24. A compound according to claim 16, wherein R² and R³ form a fused benzene ring; β is a double bond; R⁵ and R⁶ are -H; and α is a double bond:



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25. A compound according to claim 16, wherein R⁵ and R⁶ form a fused benzene ring; and α is a double bond:



26. A compound according to claim 25, wherein R² and R³ do not also form a fused ring.

27. A compound according to claim 16, wherein R⁵ and R⁶ form a fused benzene ring; α is a double bond; and R³ is -H:



10 28. A compound according to claim 16, wherein R⁵ and R⁶ form a fused benzene ring; α is a double bond; and R² is -H:



15 29. A compound according to any one of claims 1 to 28, wherein R^o is independently:

(a) -H;

(b) C₁₋₇alkyl, C₃₋₂₀heterocyclyl, or C₅₋₂₀aryl; and is optionally substituted; or;

(c) C₁₋₇alkyl-acyl, C₃₋₂₀heterocyclyl-acyl, or C₅₋₂₀aryl-acyl; and is optionally substituted.

30. A compound according to any one of claims 1 to 28, wherein R^O is independently:

(b) C_{1-7} alkyl, C_{3-20} heterocyclyl, or C_{5-20} aryl; and is optionally substituted; or:

5 (c) C_{1-7} alkyl-acyl, C_{3-20} heterocyclyl-acyl, or C_{5-20} aryl-acyl; and is optionally substituted.

31. A compound according to claim 29 or 30, wherein R^O is optionally substituted with one more of the following groups:

10 hydroxy (-OH);
halo;
carboxy (-COOH);
amino; and,
 C_{5-20} aryl.

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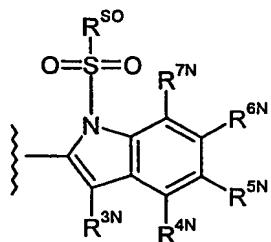
32. A compound according to claim 29 or 30, wherein R^O is unsubstituted.

33. A compound according to any one of claims 1 to 28, wherein R^O is -H.

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* * *

34. A compound according to any one of claims 1 to 33, wherein Ar is a group of the following formula:



25

wherein:

R^{SO} is independently a sulfonyl substituent; and

each of R^{3N} , R^{4N} , R^{5N} , R^{6N} , and R^{7N} is independently an indolyl substituent.

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35. A compound according to claim 34, wherein R^{SO} is C_{1-7} alkyl,
5 C_{3-20} heterocyclyl, or C_{5-20} aryl; and is optionally substituted.

36. A compound according to claim 34, wherein R^{SO} is C_{5-20} aryl; and is
optionally substituted.

10 37. A compound according to claim 34, wherein R^{SO} is C_{5-10} aryl; and is
optionally substituted.

38. A compound according to claim 34, wherein R^{SO} is C_{5-10} carboaryl; and is
optionally substituted.

15 39. A compound according to claim 34, wherein R^{SO} is phenyl or naphthyl; and
is optionally substituted.

20 40. A compound according to claim 34, wherein R^{SO} is naphthyl; and is
optionally substituted.

41. A compound according to claim 34, wherein R^{SO} is C_{5-6} carboaryl; and is
optionally substituted.

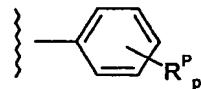
25 42. A compound according to claim 34, wherein R^{SO} is C_{5-6} aryl; and is
optionally substituted.

43. A compound according to claim 34, wherein R^{SO} is phenyl; and is optionally
substituted.

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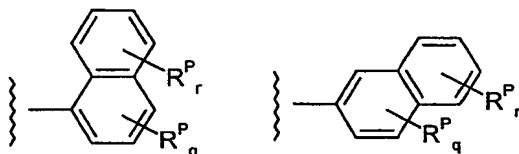
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44. A compound according to claim 34, wherein R^{SO} is:



wherein p is an integer from 0 to 5, and each R^P is a phenyl substituent.

5 45. A compound according to claim 34, wherein R^{SO} is selected from:



wherein q is an integer from 0 to 3; r is an integer from 0 to 4; and each R^P is a naphthyl substituent.

10 46. A compound according to claim 44 or 45, wherein each R^P is independently selected from:

hydroxy (-OH);
 halo;
 cyano (-CN);
 carboxy (-COOH);
 azido;
 ester;
 amino, including:

amino-C₁₋₇alkyl-amino;

20 C₁₋₇alkyl, including:

halo-C₁₋₇alkyl;
 amino-C₁₋₇alkyl;
 carboxy-C₁₋₇alkyl;
 hydroxy-C₁₋₇alkyl;

25 C₅₋₂₀aryl-C₁₋₇alkyl;

ether, including:

C₁₋₇alkoxy;
 halo-C₁₋₇alkoxy;
 amino-C₁₋₇alkoxy;

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carboxy-C₁₋₇alkoxy;

hydroxy-C₁₋₇alkoxy;

C₅₋₂₀aryl-C₁₋₇alkoxy;

acyl, including:

5 C₁₋₇alkyl-acyl;

halo-C₁₋₇alkyl-acyl;

amino-C₁₋₇alkyl-acyl;

carboxy-C₁₋₇alkyl-acyl;

hydroxy-C₁₋₇alkyl-acyl;

10 C₅₋₂₀aryl-C₁₋₇alkyl-acyl;

C₅₋₂₀aryl-acyl;

C₅₋₂₀aryl.

47. A compound according to claim 44 or 45, wherein each R^P is independently selected from:

15 -OH;

-F, -Cl, -Br, -I;

-CN;

20 -COOH;

-N₃;

-COOMe, -COOEt, -COOtBu, -COOPh, -COOCH₂Ph;

25 -NH₂, -NHMe, -NHEt, -NMe₂, -NEt₂;

piperidino, morpholino, piperazino, N-methyl-piperazino;

-NH(CH₂)_w-NH₂, -NH(CH₂)_w-NHMe, -NH(CH₂)_w-NMe₂, -NH(CH₂)_w-NEt₂;

30 -Me, -Et, -nPr, -iPr, -nBu, -iBu, -sBu, -tBu;

-CH₂F, -CH₂Cl, -CF₃, -CCl₃, -CF₂CF₃, -CH₂CF₃, -C(CF₃)₃;

-(CH₂)_w-NH₂, -(CH₂)_w-NHMe, -(CH₂)_w-NMe₂, -(CH₂)_w-NEt₂;

-(CH₂)_w-COOH;

-(CH₂)_w-OH;

-CH₂Ph;

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-OMe, -OEt, -OnPr, -OiPr, -OnBu, -OiBu, -OsBu, -OtBu;
-OCH₂F, -OCH₂Cl, -OCF₃, -OCCl₃, -OCF₂CF₃, -OCH₂CF₃, -OC(CF₃)₃;

5 -O(CH₂)_w-NH₂, -O(CH₂)_w-NHMe, -O(CH₂)_w-NMe₂, -O(CH₂)_w-NEt₂;
-O(CH₂)_w-COOH;
-O(CH₂)_w-OH;
-OCH₂Ph;

10 -C(=O)Me, -C(=O)Et, -C(=O)-nPr, -C(=O)-iPr, -C(=O)-nBu, -C(=O)-iBu,
-C(=O)-sBu, -C(=O)-tBu;
-C(=O)CH₂F, -C(=O)CH₂Cl, -C(=O)CF₃, -C(=O)CCl₃, -C(=O)CF₂CF₃,
-C(=O)CH₂CF₃, -C(=O)C(CF₃)₃;
-C(=O) (CH₂)_w-NH₂, -C(=O) (CH₂)_w-NHMe, -C(=O) (CH₂)_w-NMe₂,
-C(=O)(CH₂)_w-NEt₂;
15 -C(=O) (CH₂)_w-COOH;
-C(=O) (CH₂)_w-OH;
-C(=O)CH₂Ph;

20 -Ph;

wherein w is an integer from 1 to 7.

48. A compound according to claim 44 or 45, wherein each R^P is independently selected from: -F, -Cl, -Br, -I, -Me, -Et, -OMe, -OEt.

25 49. A compound according to claim 44 or 45, wherein each R^P is independently selected from: -F, -Me, -OMe.

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30 50. A compound according to any one of claims 34 to 49, wherein each of R^{3N}, R^{4N}, R^{5N}, R^{6N}, and R^{7N} is independently -H, or as defined for R^P.

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51. A compound according to any one of claims 34 to 49, wherein each of R^{3N} , R^{4N} , R^{5N} , R^{6N} , and R^{7N} is independently selected from: -H, -F, -Cl, -Br, -I, -Me, -Et, -OMe, -OEt.

5 52. A compound according to any one of claims 34 to 49, wherein each of R^{3N} , R^{4N} , R^{5N} , R^{6N} , and R^{7N} is independently selected from: -H, -F, -OMe.

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10 53. A compound according to any one of claims 34 to 52, wherein R^{3N} is -H.

54. A compound according to any one of claims 34 to 52, wherein each of R^{4N} and R^{7N} is -H.

15 55. A compound according to any one of claims 34 to 52, wherein each of R^{3N} , R^{4N} and R^{7N} is -H.

56. A compound according to any one of claims 34 to 52, wherein each of R^{4N} , R^{6N} , and R^{7N} is -H.

20 57. A compound according to any one of claims 34 to 52, wherein each of R^{3N} , R^{4N} , R^{6N} , and R^{7N} is -H.

25 58. A compound according to any one of claims 34 to 52, wherein each of R^{4N} , R^{5N} , and R^{7N} is -H.

59. A compound according to any one of claims 34 to 52, wherein each of R^{3N} , R^{4N} , R^{5N} , and R^{7N} is -H.

30 60. A compound according to any one of claims 34 to 52, wherein each of R^{5N} , R^{6N} , and R^{7N} is -H.

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61. A compound according to any one of claims 34 to 52, wherein each of R^{3N}, R^{5N}, R^{6N}, and R^{7N} is -H.
- 5 62. A compound according to any one of claims 34 to 52, wherein each of R^{4N}, R^{5N}, and R^{6N} is -H.
63. A compound according to any one of claims 34 to 52, wherein each of R^{3N}, R^{4N}, R^{5N}, and R^{6N} is -H.
- 10 64. A compound according to any one of claims 34 to 52, wherein each of R^{3N}, R^{4N}, R^{5N}, R^{6N}, and R^{7N} is -H.

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- 15 65. Compound SIQ-001 and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.
66. Compound SIQ-002 and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.
- 20 67. Compound SIQ-003 and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.
68. Compound SIQ-004 and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.
- 25 69. Compound SIQ-005 and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.
- 30 70. Compound SIQ-006 and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.

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71. Compound SIQ-007 and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.

5 72. Compound SIQ-008 and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.

73. Compound SIQ-009 and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.

10 74. Compound SIQ-010 and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.

75. Compound SIQ-011 and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.

15 76. Compound SIQ-012 and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.

20 77. Compound SIQ-013 and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.

* * *

25 78. A composition comprising a compound according to any one of claims 1 to 77 and a pharmaceutically acceptable carrier or diluent.

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30 78. A compound according to any one of claims 1 to 77 for use in a method of treatment of the human or animal body.

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79. Use of a compound according to any one of claims 1 to 77 for the manufacture of a medicament for use in the treatment of a proliferative condition.

5 80. Use of a compound according to any one of claims 1 to 77 for the manufacture of a medicament for use in the treatment of cancer.

10 81. Use of a compound according to any one of claims 1 to 77 for the manufacture of a medicament for use in the treatment of colon cancer or renal cancer.

15 82. Use of a compound according to any one of claims 1 to 77 for the manufacture of a medicament for use in the treatment of a condition mediated by thioredoxin/thioredoxin reductase.

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20 83. A method for the treatment of a proliferative condition comprising administering to a subject suffering from said condition a therapeutically-effective amount of a compound according to any one of claims 1 to 77.

25 84. A method for the treatment of cancer comprising administering to a subject suffering from said cancer a therapeutically-effective amount of a compound according to any one of claims 1 to 77.

85. A method for the treatment of colon cancer or renal cancer comprising administering to a subject suffering from said cancer a therapeutically-effective amount of a compound according to any one of claims 1 to 77.

30 86. A method for the treatment of a condition mediated by thioredoxin/thioredoxin reductase comprising administering to a subject suffering from said condition a therapeutically-effective amount of a compound according to any one of claims 1 to 77.

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87. A method of inhibiting thioredoxin/thioredoxin reductase in a cell, *in vitro* or
5 *in vivo*, comprising contacting said cell with an effective amount of
according to any one of claims 1 to 77.

88. A method of regulating cell proliferation, *in vitro* or *in vivo*, comprising
10 contacting a cell with an effective amount of a compound according to any
one of claims 1 to 77.

89. A method of (a) inhibiting cell proliferation; (b) inhibiting cell cycle
15 progression; (c) promoting apoptosis; or (d) a combination of one or more
of these, *in vitro* or *in vivo*, comprising contacting a cell with an effective
amount of a compound according to any one of claims 1 to 77.